

In the specification:

*On page 1, after the title, please add the following new paragraph:*

**-- RELATED APPLICATIONS**

This application is a 35 U.S.C. §371 filing of International Application Number PCT/IB2004/002165 which was filed June 30, 2004, which claims priority to U.S. Provisional Application No. 60/483691, filed on June 30, 2003. The contents of the aforementioned applications are hereby incorporated herein by reference. --

*On page 12, please replace Table 1 with the following amended Table 1:*

**Table 1**

Sequences	Name	DNA sequences	Amino acid sequences
SEQ ID N°1	RasGAP <sub>284-351</sub>	gaagatagaaggcggtacgagctattcaccta cacaataagtaccagacactgtatggaaataagttct taaaaggagatatgttcattgttcataatgaatta gaagatggatggatgtgggttacaaatattaagaac agatgaacaaggcattttgttgaagacaccttag aagaggtggccgggaagaagatccacatgaagga aaaatatggttccatggaaagatttccaaacagga agct	EDRRRVRAILPYTKV PDTDEISFLKGDMFI VHNELEDGWMWVTNL RTDEQGLIVEDLVEE VGREEDPHEGKIWFH GKISKQEA <u>(SEQ ID NO: 5)</u>
SEQ ID N°2	RasGAP <sub>284-341</sub>	gtacgagctattctacccataaaaaagtaccaga caactgtatggaaataagttttttaaaaaggagatgt tcattgttcataatgaatttttttttttttttttttt tgggttacaaatattaagaacatgttttttttttt tatttttttttttttttttttttttttttttttttt aagaagatccacatgttttttttttttttttttttt aagaagatccacatgttttttttttttttttttttt	RVRAILPYTKVPDTD EISFLKGDMFIVHNE LEDGWMWVTNLRTDE QGLIVEDLVEEVGRE EDPHEGKIW <u>(SEQ ID NO: 6)</u>
SEQ ID N°3	RasGAP <sub>284-336</sub>	gtacgagctattctacccataaaaaagtaccaga caactgtatggaaataagttttttaaaaaggagatgt tcattgttcataatgaatttttttttttttttttt tgggttacaaatattaagaacatgttttttttttt tatttttttttttttttttttttttttttttttttt	RVRAILPYTKVPDTD EISFLKGDMFIVHNE LEDGWMWVTNLRTDE QGLIVEDLVEEVGR <u>(SEQ ID NO: 7)</u>
SEQ ID N°4	RasGAP <sub>317-326</sub>	tggatgtgggttacaaatattaagaacatgt	WMWVTNLRTD <u>(SEQ ID NO: 8)</u>

*On page 12, please replace the paragraph beginning at line 12 with the following amended paragraph:*

In case the part of the SH3 domain of the N2 sequence is SEQ ID NO: 4 (RasGAP<sub>317-326</sub>) then the resulting amino acid sequence encoded by said SEQ ID NO: 4 in human is WMMWVTNLRTD (SEQ ID NO: 8). A comparison between the different species revealed that there are different amino acids, which are conserved among the species as shown in table 2.

*On pages 12-13, please replace Table 2 with the following amended Table 2:*

**Table 2**

Species	Amino acid sequences of RasGAP <sub>317-326</sub>
Human	WMMWVTNLRTD ( <u>SEQ ID NO: 8</u> )
Bos taurus	WMMWVTNLRTD ( <u>SEQ ID NO: 9</u> )
Mouse	WMMWVTNLRTD ( <u>SEQ ID NO: 10</u> )
Rattus norvegicus	WMMWVTNLRTD ( <u>SEQ ID NO: 11</u> )
Anopheles	WLWVTAHRTG ( <u>SEQ ID NO: 12</u> )
Drosophila	WLWVTAHRTG ( <u>SEQ ID NO: 13</u> )

  

Alignment	<u>WxWVTxxRTx</u> ( <u>SEQ ID NO: 14</u> )
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*On page 13, please replace the paragraph beginning at line 9 with the following amended paragraph:*

These peptidic variants of this 10 amino acid part of the human SH3 domain of N2, and in particular the alignment sequence WXWVTXXRTX (SEQ ID NO: 14), are also encompassed by the present invention and they refer to peptides having an amino acid sequence that differ to some extent from the native sequence peptide, that is the amino acid sequence that vary from the native sequence WMMWVTNLRTD (SEQ ID NO: 8) by conservative or non-conservative amino

acid substitutions, whereby one or more amino acid residues are substituted by another with same characteristics and conformational roles.

*On page 26, please replace the paragraph beginning at line 14 with the following amended paragraph:*

The HIV-TAT<sub>48-57</sub> (GRKKRRQRRR) (SEQ ID NO: 15) and TAT-RasGAP<sub>317-326</sub> (GRKKRRQRRRGWMWVTNLRTD) (SEQ ID NO: 16) peptides were synthesized at the Institute of Biochemistry, University of Lausanne, Switzerland using Fmoc technology, purified by HPLC and tested by mass spectrometry.

*On page 26, please replace the paragraph beginning at line 20 with the following amended paragraph:*

Fluorescein isothiocyanate (FITC)-labeling was performed on the sequence β-alanine-GRKKRRQRRRGWMWVTNLRTD (SEQ ID NO: 16) whose side chain Fmoc-protected amino acids were Arg(bpf), Lys(Boc), Gln(Trt), Trp(Boc), Thr(tBu), Asn(Trt), and Asp(OtBu). The peptide was synthesized stepwise on 0.2 mmol Rink Amide AM resin using Fmoc chemistry. The synthesis was monitored by ninhydrin test. After the coupling of β-alanine, the Fmoc group was removed with 20% piperidine in dimethylformamide (DMF). At this stage, a fluorescein group was conjugated to the N-terminus of peptide with FITC (5 fold excess over the substitution of the resin in 4 ml DMF and 1 ml N-ethyldiisopropylamine) to form the fluorescein-derivatized peptide.

*On page 27, please replace the paragraph beginning at line 1 with the following amended paragraph:*

The extension dn3 in the name of a plasmid indicates that the backbone plasmid is the expression vector pcDNA3 (Invitrogen). All the constructs were tagged with the HA sequence (MGYPYDVPDYAS) (SEQ ID NO: 17) at the N amino-terminal end. Plasmid N2.dn3 encodes the human RasGAP fragment N2, plasmids SH2-SH3.dn3 encodes human RasGAP amino acids

158-361, plasmids SH2.dn3 encodes human RasGAP amino acids 158-277, plasmids SH3.dn3 encodes human RasGAP amino acids 279-361. Plasmids I $\kappa$ B $\alpha$  $\Delta$ N2 encodes a form of I $\kappa$ B $\alpha$  that blocks the activation of NF $\kappa$ B (Yang and Widmann, 2002b). Plasmid pEGFP-C1, encoding the GFP protein, was from Clontech. pRL-TK, a vector encoding the *Renilla reniformis* luciferase, was from Promega. prLUC is a reporter plasmid bearing the firefly luciferase cDNA under the control of NF $\kappa$ B-responsive elements (Yang J.-Y. and Widmann C., Mol. Cell. Biol. , **21**, 5346, 2001).